

In re: Duvick, Jon P. *et al.*
Appl. No.: 10/047,825
Filed: January 16, 2002
Page 5 of 12

REMARKS

Claims 1-43 are pending in the application. Claims 1 and 6-43 are being canceled as being drawn to non-elected inventions. Applicants expressly reserve the right to file divisional applications or take such other appropriate measures deemed necessary to protect the inventions in the canceled claims. Claims 2 and 5 (and thus dependent claims 3 and 4) have been amended. Support for the amendments can be found in the specification as filed. No new matter has been added by way of amendment. Reexamination and reconsideration of the claims are respectfully requested.

Hyperlinks

The Examiner has objected to the disclosure due to the inclusion of a hyperlink on page 16, line 23. Applicants have amended the specification to remove the hyperlink, thereby obviating this objection.

Claim Objections

The Examiner has objected to claims 2-5 because the claims recite SEQ ID NOs drawn to non-elected inventions. Claims 2 and 5, and thus dependent claims 3 and 4, have been amended to remove reference to non-elected sequences. Applicants expressly reserve the right to file divisional applications or take such other appropriate measures deemed necessary to protect the sequences not currently under examination. Accordingly, Applicants respectfully request that the claim objections be withdrawn.

The Rejection of Claims 2-5 Under 35 U.S.C. §112, Second Paragraph. Should be Withdrawn

The Examiner has rejected claims 2-5 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

In re: Duvick, Jon P. *et al.*

Appl. No.: 10/047,825

Filed: January 16, 2002

Page 6 of 12

Applicants have amended claims 2 and 5, part (e), to specify hybridization and wash conditions in order to clearly define the metes and bounds of the claims. Support for this amendment can be found in the specification as originally filed on page 13, lines 19-28.

Applicants have amended claim 2 and 5, and thus dependent claims 3 and 4, according to the Examiner's suggestion of amending "peroxidase-like" activity to "peroxidase" activity. Applicants thank the Examiner for her suggestion.

Accordingly, Applicants respectfully request withdrawal of the rejections of claims 2-5 under 35 U.S.C. §112, second paragraph.

The Rejection of Claims 2-5 Under 35 U.S.C. §112, First Paragraph, Should be Withdrawn
Enablement

The Examiner has rejected claims 2-5 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Applicants respectfully disagree.

The Examiner states that the claims are broadly drawn to a nucleic acid molecule comprising any nucleotide sequence from any source comprising at least 16 contiguous bases of SEQ ID NO: 3, having at least 60% sequence identity to SEQ ID NO: 3, or that hybridizes to SEQ ID NO: 3 under unspecified stringent conditions. The Examiner asserts that the Applicants have not provided guidance for how to identify or obtain all nucleotide sequences having both the structural and functional limitations as recited in the claims, and that Applicants have not taught which regions in SEQ ID NO: 3 would tolerate modifications encompassed by the breadth of the claims. The Examiner also states that Applicants have not taught which 16 contiguous bases have the ability to encode a functional polypeptide having the desired activity. The Examiner supports her arguments using the examples of Lazar *et al.* (Mol Cell Biol, 1988, Vol. 8, No. 3, pp 1247-1257), who teach that a mutation of aspartic acid 47 and leucine 48 of a transforming growth factor alpha results in different biological activities, and Broun *et al.* (Science, 1988, Vol. 282, pp 131-133), who teach that as few as four amino acid substitutions in a protein can change the protein activity.

In re: Duvick, Jon P. *et al.*

Appl. No.: 10/047,825

Filed: January 16, 2002

Page 7 of 12

Applicants direct the Examiner's attention to Lazar *et al.*, page 1247, Abstract, which states "When aspartic acid 47 was mutated to alanine or asparagine, biological activity was retained...", thus demonstrating that not all substitutions, including non-conservative ones as noted above, impact the biological activity of a protein. Broun *et al.* actually note the high sequence similarity between the oleate 12-desaturase and oleate hydroxylase and use this to identify seven residues conserved in desaturases and to target them for modification and activity (see page 131, column 2 – column 3). Accordingly, Broun *et al.* actually use the sequence similarity of the desaturase and the hydroxylase to predict which residues to change to alter the activity of the desaturase. Thus, Broun *et al.* teach away from making amino acid substitutions that conserve function of the polypeptide as claimed by the present invention. Moreover, Broun *et al.* used common techniques to identify the critical residues of the protein and subsequently change them to destroy the function of the polypeptide. The Broun *et al.* reference therefore provides further evidence that the techniques required to generate the sequences encompassed by the instant claims are routinely used in the art. Applicants therefore assert that both the Lazar *et al.* and Broun *et al.* references use known homology to related proteins to identify and target particular amino acid residues. These references use homology to predict important conserved amino acids where substitution with another amino acid would actually be likely to have an impact on the activity of the protein. In contrast, Applicants teach precisely the opposite strategy, which is using homology to predict important conserved amino acids where substitution would *not* be likely to impact protein activity.

The specification clearly states on page 10, lines 2-6: "Guidance as to appropriate amino acid substitutions that *do not affect desired biological activity* of the native protein may be found in the model of Dayhoff *et al.* (1978) *Atlas of Protein Sequence and Structure* (Nat'l Biomed. Res. Found., Washington, D.C.), herein incorporated by reference. Conservative substitutions, such as exchanging one amino acid with another having similar properties, may be preferable." (emphasis added). The disclosure plainly acknowledges that conservative substitutions *per se*, may not produce a *functional* protein, but it is one of many tools the skilled artisan may use to produce a nucleic acid of the currently claimed invention.

In re: Duvick, Jon P. *et al.*
Appl. No.: 10/047,825
Filed: January 16, 2002
Page 8 of 12

However, in order to further prosecution, Applicants have amended claims 2 and 5 to recite 90% sequence identity to SEQ ID NO: 3. Furthermore, Applicants have amended claims 2 and 5 to recite full length nucleotide sequences comprising at least 200 contiguous nucleotides of SEQ ID NO: 3, or a nucleotide sequence encoding SEQ ID NO: 4, wherein said full length nucleotide sequence encodes a polypeptide having peroxidase activity. Applicants have also amended claims 2 and 5 to fully define stringency conditions as previously discussed in this paper.

Written Description

The Examiner has rejected claims 2-5 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner states that the Applicants have not, in fact, described all nucleotide sequences from any source having at least 60% sequence identity to SEQ ID NO: 3, or that hybridize to SEQ ID NO:3 under stringent conditions and nucleotide sequences comprising any 16 contiguous bases of SEQ ID NO: 3, and still encoding a polypeptide having peroxidase-like activity. The Examiner states that the disclosure of SEQ ID NO: 3 and nucleotide sequences encoding SEQ ID NO: 4, and other maize peroxidase enzymes described in the specification are not a representative species of the genus of the claims. In view of the claim amendments previously discussed, sequences have 60% sequence identity to SEQ ID NO: 3 or that comprise 16 contiguous bases of SEQ ID NO:3 are no longer being claimed. The amended claims recite sequences with 90% sequence identity to SEQ ID NO: 3, and full length sequences that comprise at least 200 contiguous bases of SEQ ID NO: 3.

The recitation of at least 90% sequence identity, as recited in claims 2 and 5, is a very predictable structure of the sequences encompassed by the claimed invention. Satisfactory disclosure of a representative number of species depends on whether one of skill in the art would recognize that Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Guidelines

In re: Duvick, Jon P. *et al.*

Appl. No.: 10/047,825

Filed: January 16, 2002

Page 9 of 12

for Examination of Patent Applications Under 35 U.S.C. §112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (January 5, 2001). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a sequence having at least 90% sequence identity to the sequence set forth in SEQ ID NO: 3.

Similarly, the recitation of a full length nucleotide sequence having at least 200 contiguous nucleotides of SEQ ID NO: 3, as recited in claims 2 and 5, is a very predictable structure of the sequences encompassed by the claimed invention. Moreover, these claims recite that the nucleotide sequence encodes a full-length peroxidase polypeptide. Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a nucleotide sequence having at least 200 contiguous nucleotides of SEQ ID NO: 3 and encoding a full-length peroxidase polypeptide.

The Examiner is again reminded that the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 U.S.P.Q.2d 1662, 1669 (Bd. Pat. App. & Int. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by a nucleotide sequence, falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also*, Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. at 1106. The recitation in claims 2 and 5 of a predictable structure of at least 90% sequence identity to SEQ ID NO: 3 is sufficient to satisfy the written description requirement. Similarly, the recitation in claims 2 and 5 of a predictable structure of at least 200 contiguous nucleotides of SEQ ID NO: 3, wherein the nucleotide sequence encodes a full-length peroxidase polypeptide, is also sufficient to satisfy the written description requirement.

In re: Duvick, Jon P. *et al.*
Appl. No.: 10/047,825
Filed: January 16, 2002
Page 10 of 12

Moreover, an Applicant may rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *Id.*, citing *Lilly* at 1568. Claims 2 and 5 have been amended to replace "peroxidase-like activity" with "peroxidase activity". Thus, claims 2 and 5 (and thus dependent claims 3 and 4) recite that the claimed sequences encode a polypeptide having peroxidase activity, thereby providing a functional characterization of the sequences claimed in each genus.

Applicants have given clear guidance of hybridization conditions and requirements as discussed *supra*. Furthermore, Applicants have amended the claims to clearly specify the hybridization conditions required. As such, the written description is clearly adequate and commensurate with the claims.

Accordingly, Applicants request that the rejection of claims 2-5 under 35 U.S.C. §112, first paragraph, be withdrawn.

The Rejection of Claim 2 Under 35 U.S.C. §102 Should be Withdrawn

The Examiner has rejected claim 2 under 35 U.S.C. §102(b) as being anticipated by Shen *et al.* (Accession No. T18410, Oct. 1996). The Examiner states that Shen *et al.* teach an isolated cDNA from maize comprising at least 150 contiguous bases of SEQ ID NO:3, encoding a polypeptide having peroxidase activity. The sequence disclosed by Shen *et al.* is clearly annotated as being a 5' end of a sequence, and is therefore not full length. Although the sequence is annotated as having homology to known peroxidase genes, the sequence disclosed by Shen *et al.* has not been shown to have peroxidase activity. Shen *et al.* do not teach, disclose or suggest the full length sequence set forth in SEQ ID NO:3. Accordingly, in view of the claim amendments removing reference to nucleotide sequences comprising 16 contiguous nucleotide bases of SEQ ID NO: 3, and furthermore in view of the fact that the sequence disclosed by Shen *et al.* is a fragment that has not been shown to have any functional activity, Applicants assert that the Shen *et al.* reference does not anticipate claim 2.

In re: Duvick, Jon P. *et al.*
Appl. No.: 10/047,825
Filed: January 16, 2002
Page 11 of 12

In view of the preceding remarks and claim amendments, Applicants respectfully request withdrawal of the rejection of claim 2 under 35 U.S.C. §102.

The Rejection of Claims 2-5 Under 35 U.S.C. §103 Should be Withdrawn

The Examiner states that it is presumed that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicants hereby confirm for the Examiner that the subject matter of the various claims was indeed commonly owned at the time the inventions covered therein were made.

The Examiner has rejected claims 2-5 under 35 U.S.C. §103(a) as being unpatentable over Ross, A.H. (Accession No. U12314; Thesis, Botany, University of Queensland). Ross teaches an isolated nucleic acid molecule that comprises at least 60 contiguous bases of SEQ ID NO:3 and encoding a polypeptide having peroxidase activity. Ross does not teach, disclose or suggest the sequence set forth in SEQ ID NO:3, nor does Ross teach, disclose or suggest a full length gene sequence having 200 or more contiguous nucleotides of SEQ ID NO: 3 which encodes a peroxidase. In view of the claim amendments removing reference to nucleotide sequences comprising 16 contiguous bases of SEQ ID NO: 3, Applicants assert that the Ross reference cannot be used to motivate one of skill in the art to transform a plant host cell with the peroxidase nucleotide sequence disclosed in SEQ ID NO: 3, or a full length gene sequence having 200 or more contiguous nucleotides of SEQ ID NO: 3.

Accordingly, Applicants request the withdrawal of the rejections of claims 2-5 under 35 U.S.C. §103(a).

CONCLUSION

In view of the above amendments and remarks, Applicants submit that the rejections of the claims under 35 U.S.C. §112, first and second paragraphs, 35 U.S.C §102 and 35 U.S.C. §103 have been overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

In re: Duvick, Jon P. *et al.*
Appl. No.: 10/047,825
Filed: January 16, 2002
Page 12 of 12

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR §1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-1852.

Respectfully submitted,

Claire L. Moxon

Claire L. Moxon

Agent for Applicant(s)

(See: LIMITED RECOGNITION
UNDER 37 CFR § 10.9(b)
SUBMITTED 6-17-2003)

PIONEER HI-BRED INTERNATIONAL, INC.
Corporate Intellectual Property
7100 N.W. 62nd Avenue
P.O. Box 1000
Johnston, Iowa 50131-1000
Phone: (515) 253-2162
Facsimile: (515) 334-6883

RECEIVED
CENTRAL FAX CENTER
SEP 22 2003

OFFICIAL